CLAIMS

We claim:

1. A therapeutic agent carrier, comprising:

(a) a reversible geling copolymer, having a linear random copolymer of:

(i) an N-alkyl substituted [meth-]acrylamide derivitive; and

(ii) a hydrophilic comonomer, wherein an amount of said hydrophilic comonomer in the linear random copolymer is less than about 10 mole% wherein gelation occurs with substantially no synerisis,

said linear random copolymer in the form of a plurality of linear chains having a plurality of molecular weights greater than or equal to a minimum geling molecular weight cutoff, and excluding a substantial amount of copolymer chains or polymer chains having molecular weights less than the minimum geling molecular weight cutoff;

(b) an aqueous solvent mixed with said reversible geling copolymer as a reversible geling solution; and

(c) a therapeutic agent mixed with said reversible geling solution as said therapeutic agent carrier.

2. The therapeutic agent carrier as recited in claim 1, wherein said amount is from about 1.6 mole% to about 2 mole%.

3. The therapeutic agent carrier as recited in claim 1, wherein said N-alkyl substituted [meth-]acrylamide is

selected from the group consisting of N-isopropyl[meth-]acrylamide, N,N-diethyl[meth-]acrylamide, N-[meth-]acryloylpyrrolidine, N-ethyl[meth-]acrylamide, and combinations thereof.

4. The therapeutic agent carrier as recited in claim 1, wherein said hydrophilic comonomer is hydrophilic [meth-]acryl- compound.

5. The therapeutic agent carrier as recited in claim 4, wherein said hydrophilic [meth-]acryl- compound is selected from the group consisting of carboxylic acid, [meth-]acrylamide, hydrophilic [meth-]acrylic acid ester, hydrophilic [meth-]acrylamide derivatives and combinations thereof.

6. The therapeutic agent carrier as recited in claim 5, wherein said carboxylic acid is selected from the group consisting of acrylic acid, methacrylic acid and combinations thereof.

7 The therapeutic agent carrier as recited in claim 6, wherein said hydrophilic [meth-]acrylamide derivatives are selected from the group consisting of N,N-diethyl[meth-]acrylamide, 2-[N,N-dimethylamino]ethyl[meth-]acrylamide, 2-[N,N-diethylamino]ethyl[meth-]acrylamide, or combinations thereof.

8. The therapeutic agent carrier as recited in claim 5, wherein said hydrophilic [meth-]acrylic ester is selected from the group consisting of 2-[N,N-diethylamino]ethyl[meth-

]acrylate, 2-[N,N-dimethylamino]ethyl[meth-]acrylate, and combinations thereof.

9. The therapeutic agent carrier as recited in claim 1, wherein said aqueous solvent is selected from the group consisting of water, and aqueous salt solution.

10. The therapeutic agent carrier as recited in claim 9, wherein said salt solution is a phosphate buffered saline.

11. The therapeutic agent carrier as recited in claim 10, wherein an amount of said solvent is from about 70 wt% to about 99 wt%.

12. The therapeutic agent carrier as recited in claim 1, wherein said therapeutic agent is selected from the group consising of anti-cancer agents, hormones, antibiotics, narcotic antagonists, analgesics, anti-inflammatory agents, anti-depressant, anti-epileptic, anti-malarial agents, immunoactivators, growth factors, gene therapy agents, oligonucleotides, therapeutic peptides and proteins, chemo-embolic material and combinations thereof.

13. A method of making a therapeutic agent carrier, comprising the steps of:

(a) mixing an N-alkyl substituted [meth-]acrylamide derivitive with a hydrophilic comonomer in a reaction solvent with an initiator forming a reaction mixture, wherein an amount of said hydrophilic comonomer in the linear random copolymer is less than about 10 mole

wherein gelation occurs with substantially no synerisis;

(b) copolymerizing the reaction mixture and forming a first linear random copolymer having a plurality of linear chains having a plurality of molecular weights greater than or equal to a minimum geling molecular weight cutoff, and excluding a substantial amount of copolymer chains or polymer chains having molecular weights less than the minimum geling molecular weight cutoff;

(c) isolating and purifying the copolymerized first linear random copolymer and obtaining a second linear random copolymer

(d) mixing the thermally reversible copolymer with an aqueous solvent and making a reversible geling solution; and

(e) adding a therapeutic agent and obtaining said therapeutic agent carrier.

14. The method as recited in claim 13 wherein said initiator is a free radical initiator.

15. The method as recited in claim 13, wherein said amount is from about 1.6 mole% to about 2 mole%.

16. The method as recited in claim 13, wherein said N-alkyl substituted [meth-]acrylamide is selected from the group consisting of N-isopropyl[meth-]acrylamide, N,N-diethyl[meth-]acrylamide, N-[meth-]acryloylpyrrolidine, N-ethyl[meth-]acrylamide, and combinations thereof.

17. The method as recited in claim 13, wherein said hydrophilic comonomer is hydrophilic [meth-]acryl- compound.

18. The method as recited in claim 17, wherein said hydrophilic [meth-]acryl- compound is selected from the group consisting of carboxylic acid, [meth-]acrylamide, hydrophilic [meth-]acrylic acid ester, hydrophilic [meth-]acrylamide derivatives and combinations thereof.

19. The method as recited in claim 18, wherein said carboxylic acid is selected from the group consisting of acrylic acid, methacrylic acid and combinations thereof.

20. The method as recited in claim 18, wherein said hydrophilic [meth-]acrylamide derivatives are selected from the group consisting of N,N-diethyl[meth-]acrylamide, 2-[N,N-dimethylamino]ethyl[meth-]acrylamide, 2-[N,N-diethylamino]ethyl[meth-]acrylamide, or combinations thereof.

21. The method as recited in claim 18, wherein said hydrophilic [meth-]acrylic ester is selected from the group consisting of 2-[N,N-diethylamino]ethyl[meth-]acrylate, 2-[N,N-dimethylamino]ethyl[meth-]acrylate, and combinations thereof.

22. The method as recited in claim 13, wherein said reaction solvent is selected from the group consisting of aqueous solvent, hydrocarbon solvent, and combinations thereof.

23. The method as recited in claim 22, wherein said aqueous solvent is selected from the group consisting of

water, aqueous salt solution and combinations thereof.

24. The method as recited in claim 22, wherein said hydrocarbon solvent is selected from the group consisting of oxygenated hydrocarbon, chlorinated hydrocarbon, aromatic hydrocarbon, and combinations thereof.

25. The method as recited in claim 24, wherein said oxygenated hydrocarbon is dioxane.

26. The method as recited in claim 24, wherein said chlorinated hydrocarbon is chloroform.

27. The method as recited in claim 24, wherein said aromatic hydrocarbon is benzene.

28. The method as recited in claim 13, wherein said aqueous solvent is selected from the group consisting of water, and aqueous salt solution.

29. The method as recited in claim 28, wherein said salt solution is a phosphate buffered saline.

30. The method as recited in claim 13, wherein said therapeutic agent carrier is selected from the group consising of is selected from the group consising of anti-cancer agents, hormones, antibiotics, narcotic antagonists, analgesics, anti-inflammatory agents, anti-depressant, anti-epileptic, anti-malarial agents, immunoactivators, growth factors, gene therapy agents, oligonucleotides, therapeutic

peptides and proteins, chemo-embolic material and combinations thereof.

31. A biodegradable thermally reversible graft copolymer, comprising:

(a) a biodegradable polymer; grafted with

(b) a side chain selected from the group consisting of homo-oligomers of [meth-]acrylamide derivatives, co-oligomers of [meth-]acrylamide derivatives, homo-oligomers of [meth-]acrylamide derivatives copolymerized with hydrophilic comonomers, co-oligomers of [meth-]acrylamide derivatives copolymerized with hydrophilic comonomers.

32. The copolymer as recited in claim 31, wherein said biodegradable copolymer is selected from the group consisting of polyaminoacids, poly(phosphasenes), poly(caprolactone), polypeptides, polysaccharides and combinations thereof.

33. The copolymer as recited in claim 31, wherein said oligo [meth-]acrylamide derivative is an N-alkyl substituted [meth-] acrylamide derivative.

34. The copolymer as recited in claim 31, wherein said oligo [meth-]acrylamide derivative side chain is randomly copolymerized with a hydrophilic comonomer as a linear random oligomer, said linear random oligomer having molecular weight less than a minimum geling molecular weight cutoff.

35. A reversible geling copolymer solution, comprising the copolymer as recited in claim 31, mixed with an aqueous solvent.

36. A therapeutic agent carrier, comprising:

the copolymer solution as recited in claim 35, mixed with a therapeutic agent.

37. A method of making a biodegradable thermally reversible copolymer, comprising the steps of:

(a) polymerizing a plurality of side chains selected from the group consisting of homo-oligomers of [meth-]acrylamide derivatives, co-oligomers of [meth-]acrylamide derivatives, homo-oligomers of [meth-]acrylamide derivatives copolymerized with hydrophilic comonomers, co-oligomers of [meth-]acrylamide derivatives copolymerized with hydrophilic comonomers, said side chain having a first active group; and

(b) coupling the side chains to a biodegradable polymer having a plurality of second active groups wherein said first active group connects to one of the plurality of the second active groups.

38. The method as recited in claim 37, wherein said biodegradable polymer is selected from the group consisting of polyaminoacid, poly(phosphazenes), poly(caprolactone), polypeptides, polysaccharides and combinations thereof.

39. The method as recited in claim 37, wherein said polymerizing is a free radical copolymerization wherein the first active group is an amino which originates from an amino-terminated chain transfer agent.

40. The method as recited in claim 39, wherein said amino-terminated chain transfer agent is 2-aminoethanethiol hydrochloride.

41. The method as recited in claim 37, wherein said coupling is with an activation reagent.

42. The method as recited in claim 39, wherein said activation reagent is dicyclohexyl carbodiimide.

43. The method as recited in claim 37, wherein said oligo [meth-]acrylamide derivative is an N-alkyl substituted [meth-] acrylamide derivative.

44. The method as recited in claim 37, wherein said oligo [meth-]acrylamide derivative side chain is randomly copolymerized with a hydrophilic comonomer as a linear random oligomer, said linear random oligomer having molecular weight less than a minimum geling molecular weight cutoff.

45. The method as recited in claim 37, further comprising the step of:

mixing the biodegradable copolymer with an aqueous solvent.

46. The method as recited in claim 45, further comprising the step of:

adding a therapeutic agent and obtaining a therapeutic agent carrier.